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=> s vaudry hubert /au
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command can only be used to look at the index in a file which has an
index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file medline biosis embase caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 14:47:16 ON 10 MAR 2004

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=> s vaudry hubert /au L1 656 VAUDRY HUBERT

=> s chartrei nicolas /au L2 0 CHARTREI NICOLAS

=> s beaudet alain /au L3 187 BEAUDET ALAIN

=> s hungarian lenkei/au

L4 0 HUNGARIAN LENKEI/AU

=> s (compound (s) library) (p) internali? (p) gpcr (p) fluores?

L6 0 (COMPOUND (S) LIBRARY) (P) INTERNALI? (P) GPCR (P) FLUORES?

=> s library) (p) internali? (p) gpcr (p) fluores?
UNMATCHED RIGHT PARENTHESIS 'LIBRARY) '
The number of right parentheses in a query must be equal to the number of left parentheses.

=> dup rem 17
PROCESSING COMPLETED FOR L7
L8 1 DUP REM L7 (3 DUPLICATES REMOVED)

=> d 18 ibib kwic

L8 ANSWER 1 OF 1 MEDLINE ON STN ACCESSION NUMBER: 2002461764 MEDLINE DUPLICATE 1

PubMed ID: 12220620 DOCUMENT NUMBER:

Sphingosine 1-phosphate is a ligand of the human gpr3, gpr6 TITLE:

and qpr12 family of constitutively active G protein-coupled

Uhlenbrock Kirsten; Gassenhuber Hans; Kostenis Evi AUTHOR: CORPORATE SOURCE:

Aventis Pharma Germany, Disease Group Cardiovascular,

Industriepark Hochst, Frankfurt/Main, Germany...

kirsten.uhlenbrock@aventis.com

Cellular signalling, (2002 Nov) 14 (11) 941-53. SOURCE:

Journal code: 8904683. ISSN: 0898-6568.

England: United Kingdom PUB. COUNTRY:

Journal; Article; (JOURNAL ARTICLE) DOCUMENT TYPE:

LANGUAGE: English

Priority Journals FILE SEGMENT:

200304 ENTRY MONTH:

Entered STN: 20020911 ENTRY DATE:

Last Updated on STN: 20030419 Entered Medline: 20030418

Five G protein-coupled receptors (GPCRs) for the ΔB lysophospholipid sphingosine 1-phosphate (S1P) have been cloned and characterized so far. We report here about the identification of gpr3, gpr6 and gpr12 as additional members of the S1P-GPCR family. When expressed transiently in HEK293 cells, gpr3, gpr6 and gpr12 confer constitutive activation of adenylate cyclase (AC) similar in. . . in medium with charcoal-stripped serum (devoid of lipids) significantly reduces cyclic adenosine monophosphate (cAMP) levels, suggesting a lipid-like ligand. A library containing 200 bioactive lipids was applied in functional assays recording intracellular Ca(2+) mobilization. S1P and dihydrosphingosine 1-phosphate (DHS1P) were identified. . . of AC is enhanced; and (ii) overexpression of G(alpha)(i) significantly reduces the stimulatory action on intracellular cAMP levels. Agonist (S1P)-mediated internalization can be visualized in intact HEK293 cells using a gpr6 green fluorescent protein (GFP) fusion protein. In summary, our data suggest that gpr3, gpr6 and gpr12 are a family of constitutively active. . .

=> s screen? (p) internali? (p) gpcr (p) fluores? Ь9 12 SCREEN? (P) INTERNALI? (P) GPCR (P) FLUORES?

=> dup rem 19

PROCESSING COMPLETED FOR L9

4 DUP REM L9 (8 DUPLICATES REMOVED) L10

=> d l10 total ibib kwic

L10 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:931468 CAPLUS

DOCUMENT NUMBER: 140:13002

TITLE: Screening for effectors of G protein-coupled receptor

internalization by measuring the effects of test

substances on distribution of components of the signal

transduction mechanism

INVENTOR(S): Oakley, Robert H.; Hudson, Christine C.

Norak Biosciences, Inc., USA PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 127 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE -----A2 20031127 WO 2003097795 WO 2003-US14581 20030512

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2002-379986P P 20020513 PRIORITY APPLN. INFO.: US 2002-401698P P 20020807 TT Proteins RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (green fluorescent, fusion products with arrestins; screening for effectors of GPCR

> internalization by measuring effects of test substances on distribution of components of signal transduction mechanism)

L10 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2001018413 MEDLINE DOCUMENT NUMBER: PubMed ID: 10907092

TITLE: Cell-based, high-content screen for receptor

internalization, recycling and intracellular trafficking.
Ghosh R N; Chen Y T; DeBiasio R; DeBiasio R L; Conway B R;

AUTHOR: Ghosh R N; Chen Y T; De Minor L K; Demarest K T

CORPORATE SOURCE: Cellomics Inc., Pittsburgh, PA, USA.

SOURCE: BioTechniques, (2000 Jul) 29 (1) 170-5.

Journal code: 8306785. ISSN: 0736-6205.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200011

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322 Entered Medline: 20001109

AB A variety of physiologically important receptors are internalized and then recycled back to the plasma membrane by the endocytic recycling compartment. These include the transferrin receptor and many G-protein coupled receptors (GPCRs). The internalization of GPCRs is a result of agonist stimulation. A cell-based fluorescent imaging assay is described that detects and quantifies the presence of fluorescently labeled receptors and macromolecules in the recycling compartment. This High Content Screening application is conducted on the ArrayScan II System that includes fluorescent reagents, imaging instrumentation and the informatics tools necessary to screen for compounds that affect receptor internalization, recycling and GPCR activation. We demonstrate the Receptor Internalization and Trafficking application by quantifying (i) the internalization and recycling of the transferrin receptor using a fluorescently labeled ligand and (ii) the internalization of a physiologically functional model GPCR, a GFP-parathyroid hormone receptor chimera. These assays give high signal-to-noise ratios, broad dynamic ranges between stimulated and unstimulated conditions and low variability across different screening runs. Thus, the Receptor Internalization and Trafficking application, in conjunction with the ArrayScan II System, forms the basis of a robust, information-rich and automated screen for GPCR activation.

L10 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 2

ACCESSION NUMBER: 1999:281319 BIOSIS DOCUMENT NUMBER: PREV199900281319

TITLE: Quantification of G-protein coupled receptor

internalization using G-protein coupled receptor-green fluorescent protein conjugates with the ArrayScanTM

high-content screening system.

AUTHOR(S): Conway, Bruce R. [Reprint author]; Minor, Lisa K.; Xu, Jun

Z.; Gunnet, Joseph W.; DeBiasio, Robbin; D'Andrea, Michael R.; Rubin, Richard; DeBiasio, Richard; Giuliano, Ken; Zhou,

Lubing; Demarest, Keith T.

CORPORATE SOURCE: R.W. Johnson Pharmaceutical Research Institute, 1000 Route

202, Room B-122, Raritan, NJ, 08869, USA

SOURCE: Journal of Biomolecular Screening, (April, 1999) Vol. 4,

No. 2, pp. 75-86. print.

ISSN: 1087-0571.

DOCUMENT TYPE:

Article English

LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jul 1999

Last Updated on STN: 28 Jul 1999

AB Many G-protein coupled receptors (GPCRs) undergo

ligand-dependent homologous desensitization and internalization.

Desensitization, defined as a decrease in the responsiveness to ligand, is

accompanied by receptor aggregation on the cell surface and internalization via clathrin-coated pits to an intracellular

endosomal compartment. In this study, we have taken advantage of the

trafficking properties of GPCRs to develop a useful

screening method for the identification of receptor mimetics. A series of studies were undertaken to evaluate the expression, functionality, and ligand-dependent trafficking of GPCR-green fluorescent protein (GFP) fusion conjugates stably transfected into HEK 293 cells. These GPCR-GFP expressing cells were then

utilized in the validation of the ArrayScanTM (CellomicsTM, Pittsburgh, PA), a microtiter plate imaging system that permits cellular and subcellular quantitation of **fluorescence** in whole cells. These studies demonstrated our ability to measure the **internalization** of a parathyroid hormone (PTH) receptor-GFP conjugate after ligand

treatment by spatially resolving internalized receptors.

Internalization was time- and dose-dependent and appeared to be selective for PTH. Similar results were obtained for a beta2-adrenergic receptor (beta2 AR)-GFP conjugate stably expressed in HEK 293 cells. The internalized GFP-labeled receptors were visualized as numerous punctate "spots" within the cell interior. An algorithm has been developed that identifies and collects information about these spots, allowing quantification of the internalization process.

Variables such as the receptor-GFP expression level, plating density, cell number per field, number of fields scanned per well, . . . spot size,

and spot intensity were evaluated during the development of this assay. The method represents a valuable tool to **screen** for receptor mimetics and antagonists of receptor **internalization** in whole

cells rapidly.

SOURCE:

L10 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 1998244535 MEDLINE DOCUMENT NUMBER: PubMed ID: 9585136

TITLE: Molecular mechanisms of G protein-coupled receptor

desensitization and resensitization.

AUTHOR: Ferguson S S; Zhang J; Barak L S; Caron M G

CORPORATE SOURCE: John P. Robarts Research Institute and Department of

Physiology, University of Western Ontario, London. Life sciences, (1998) 62 (17-18) 1561-5. Ref: 22

Journal code: 0375521. ISSN: 0024-3205.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

199805

ENTRY DATE:

Entered STN: 19980609

Last Updated on STN: 20000303 Entered Medline: 19980526

Beta-arrestin proteins play a dual role in regulating G protein-coupled AB receptor (GPCR) responsiveness by contributing to both receptor desensitization and internalization. Recently, beta-arrestins were also shown to be critical determinants for beta2-adrenergic receptor (beta2AR) resensitization. This was demonstrated by overexpressing wild-type. . . cell types was shown to be dependent upon beta-arrestin expression levels. To further study the mechanisms underlying beta-arrestin function, green fluorescent protein was coupled to beta-arrestin2 (beta arr2GFP), thus allowing the real-time visualization of the agonist-dependent trafficking of beta-arrestin in living. . from the most sensitive second messenger readout systems. Beta arr2GFP translocation was GRK-dependent and was demonstrated for 16 different ligand-activated GPCRs. Because beta-arrestin binding is a common divergent step in GPCR signalling, this assay represents a universal methodology for screening orphan receptors, GRK inhibitors and novel GPCR ligands. Moreover, beta arr2GFP provides a valuable new tool to dissect the biological function and regulation of beta-arrestin proteins.

=> log y COST IN U.S. DOLLARS

SINCE FILE

TOTAL

FULL ESTIMATED COST

ENTRY SESSION 47.10 47.31

STN INTERNATIONAL LOGOFF AT 14:55:48 ON 10 MAR 2004

L Number	Hits	Search Text	DB	Time stamp
2	281	(peptide same library) and internali\$7 and gpcr and (fluores\$8 same label)	USPAT;	2004/03/10 11:09
			US-PGPUB;	
			EPO; JPO;	
			DERWENT	
1	322	(peptide same library) and internali\$7 and gpcr and fluores\$8	USPAT;	2004/03/10 11:21
			US-PGPUB;	
			EPO; JPO,	
			DERWENT	
3	0	(compund same library) and internali\$7 and gpcr and fluores\$8	USPAT;	2004/03/10 11:22
			US-PGPUB;	
			EPO; JPO;	
			DERWENT	
4	333	(compound same library) and internali\$7 and gpcr and fluores\$8	USPAT;	2004/03/10 11:24
			US-PGPUB;	
			EPO; JPO;	
			DERWENT	
5	388	screen\$7 and internali\$7 and gpcr and fluores\$8	USPAT;	2004/03/10 11:35
		.	US-PGPUB;	
			EPO; JPO;	
			DERWENT	
6	3	vaudry-hubert.in.	USPAT;	2004/03/10 11:35
			US-PGPUB;	
			EPO; JPO;	
			DERWENT	
7	0	chartrei-nicolas.in.	USPAT;	2004/03/10 11:36
		,	US-PGPUB;	
			EPO; JPO;	
			DERWENT	
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			EPO; JPO;	
			DERWENT	
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10	7	llorens-cortes-catherine.in.	USPAT;	2004/03/10 11:36
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			DERWENT	